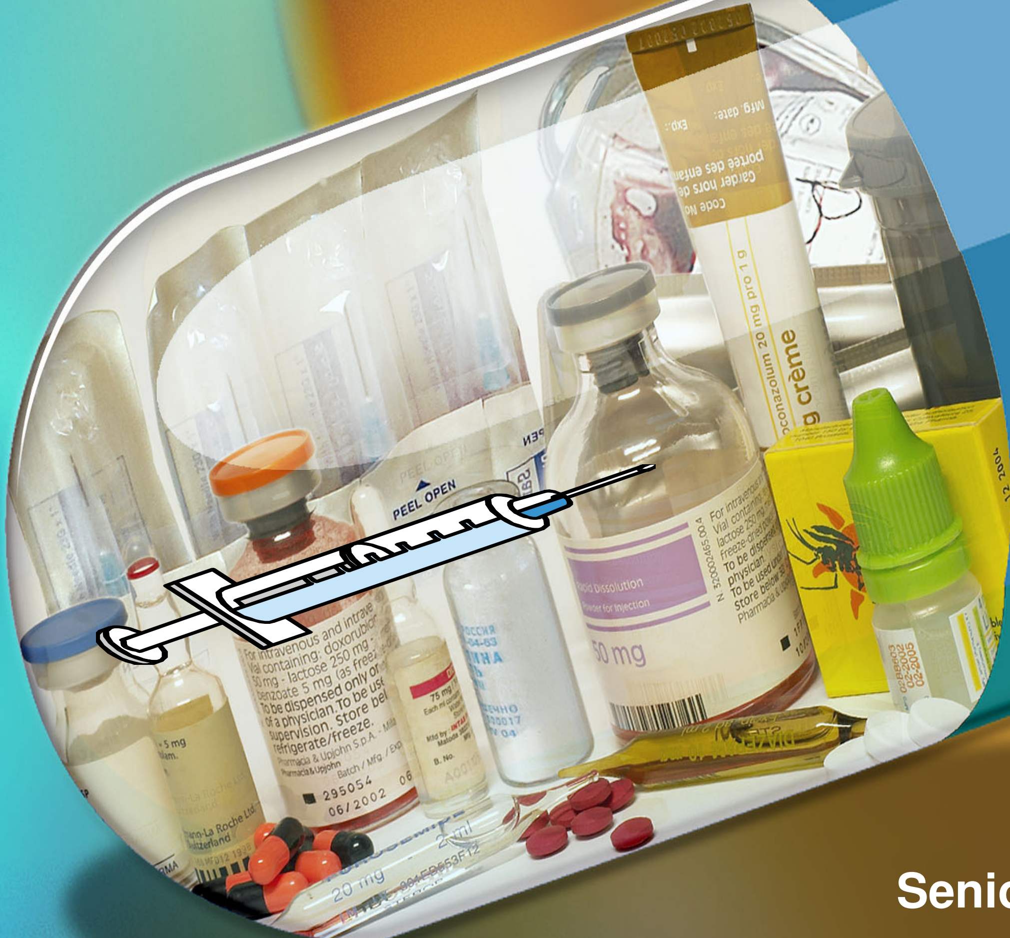


Global Vaccine Market Features and Trends

Miloud Kaddar

Senior Adviser, Health Economist

WHO, IVB, Geneva

Global Vaccine Market

- Differences between vaccines and medicines
- Main features of the vaccine market
- New trends since 2000?
- Implications for GAVI graduating and middle income countries?

VACCINES VERSUS DRUGS

Vaccines	Medicines
Healthy People	Generally Sick People
High Risk Aversion	Moderate Risk Aversion
Induced Demand	Individual and Mixed Demand
Importance of UN, NITAG & Govt. Recommendations	Importance of Prescribers & Medical Societies
Public Funding (Govt, UN Donors)	High share of out of pocket and Health Insurance
Low mark up and taxes	Possible high mark up and taxes
No generics	Generics
Public good, positive externalities	Variable
Politically and Media sensitive	Variable

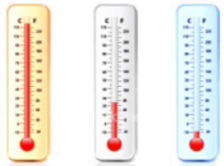
Key differences between vaccines and drugs

Preventive	vs.	Therapeutic
Biologics		Small molecules
Biosimilars		Generics
Process patents		Product patents
High capital costs		Lower capital costs
Long and complex manufacturing		Manufacturing relatively simple
Very large clinical trials		Smaller clinical trials
Limited secondary market		Often significant secondary market

Seth Berkley, GAVI

Vaccines are not commodity products and should not be treated as such (UNICEF SD)

Vaccine Product Profile



High Product Sensitivity

- Biological products
- Significant risks of production failures
- Quality is the OVER-RIDING criterion
- Highly regulated production environment
- Dependency on well functioning NRA
- Requiring constant temperature control ⇔ Cold Chain from Manufacturer to End user
- Limited shelf life

Limited Supply

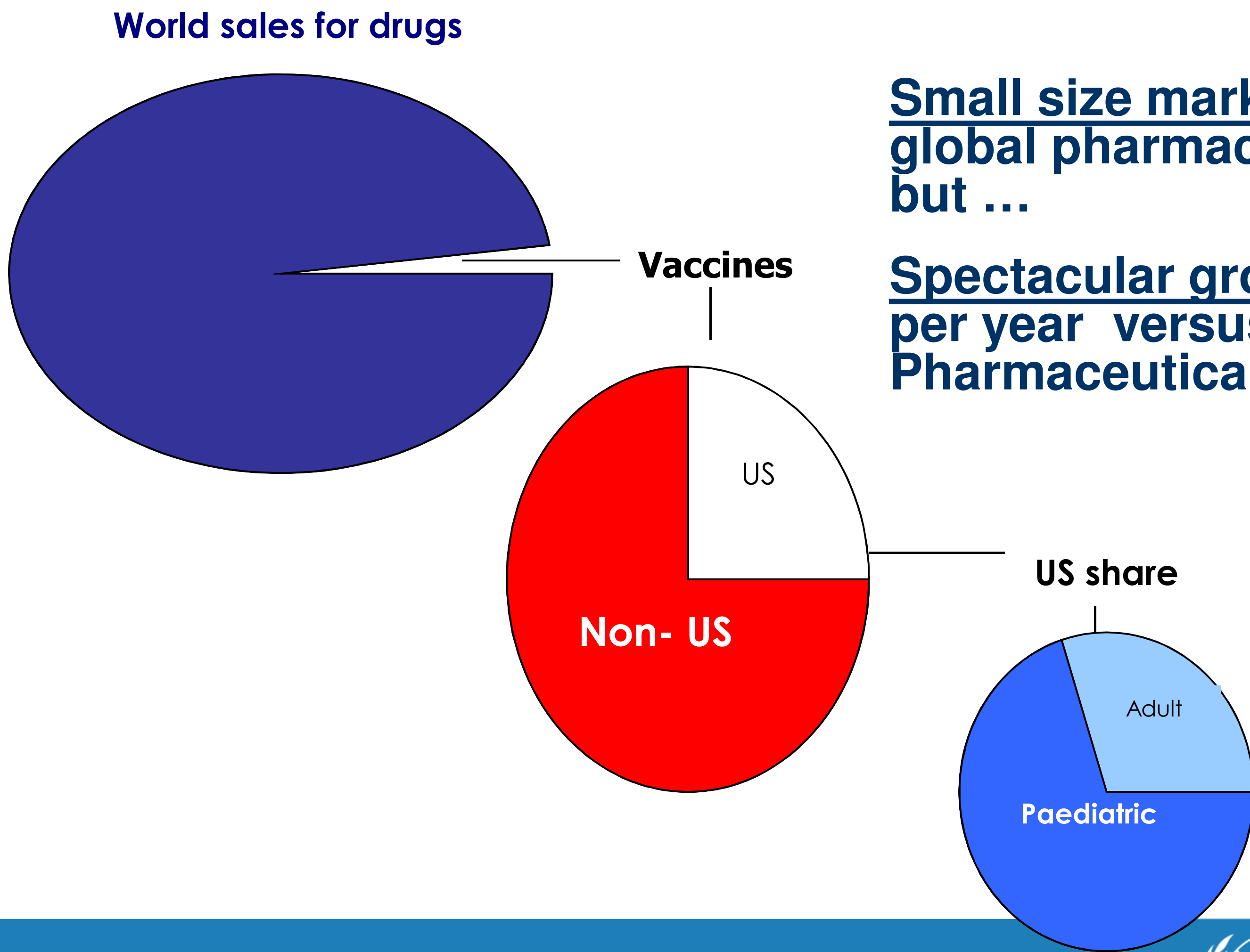
- 1- 5 suppliers per product
- High entry cost to manufacturers
- Diverse dynamics in individual vaccine markets
- New vaccines often result in monopoly supply

Vaccine production and Market Competition

- Production of a dose: 6 -24 Months
- Capacity Increase: 2-3 years
- New Plant: 5-7 years
- New regulatory requirements can cause interruptions
- New vaccines being introduced globally, global competition
- Initial selection has long term impact

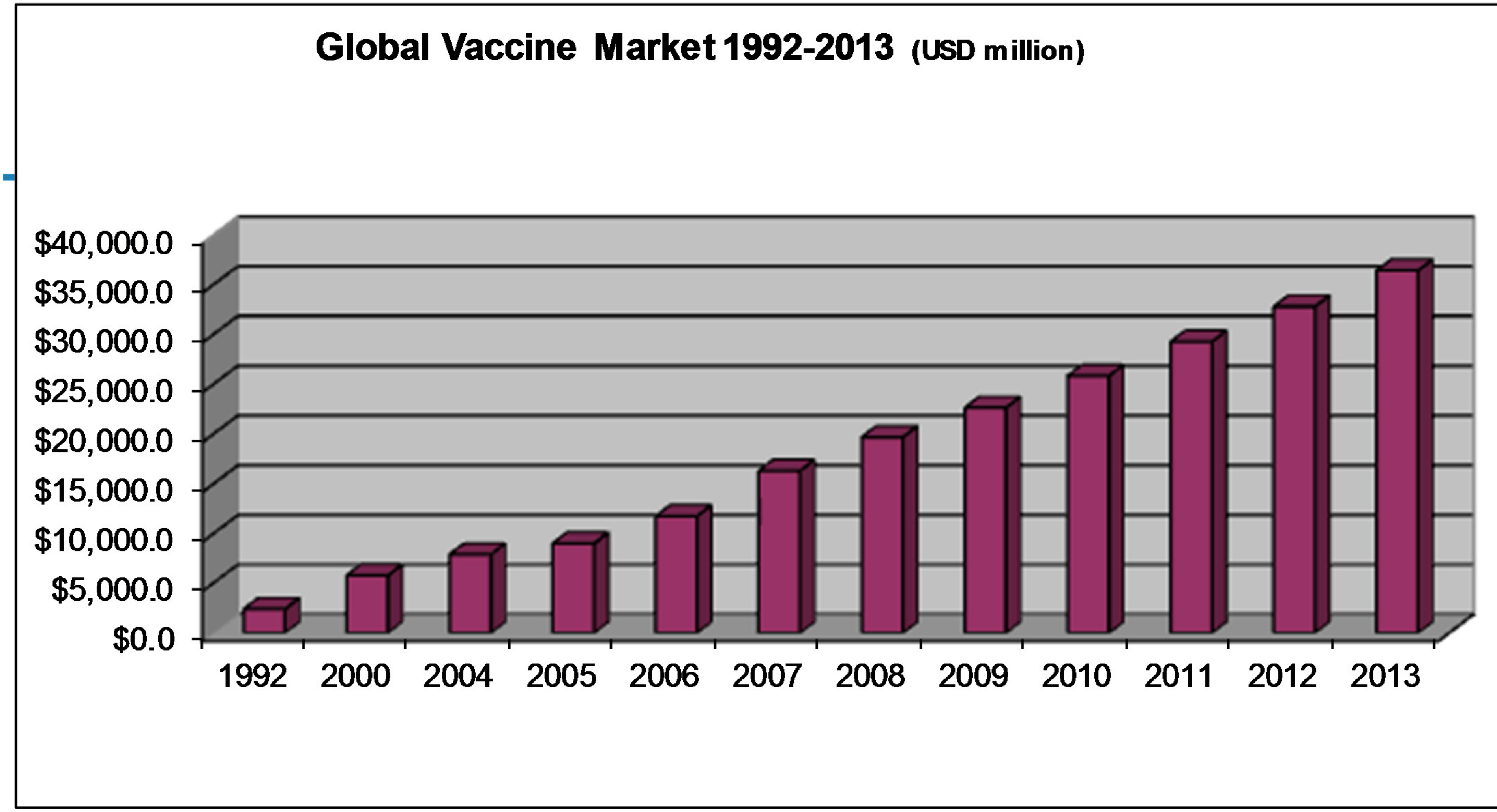
Requiring a specific approach to be developed for vaccine procurement

VACCINE MARKET STRUCTURE 2010



Small size market : 2-3% of the global pharmaceutical market but …

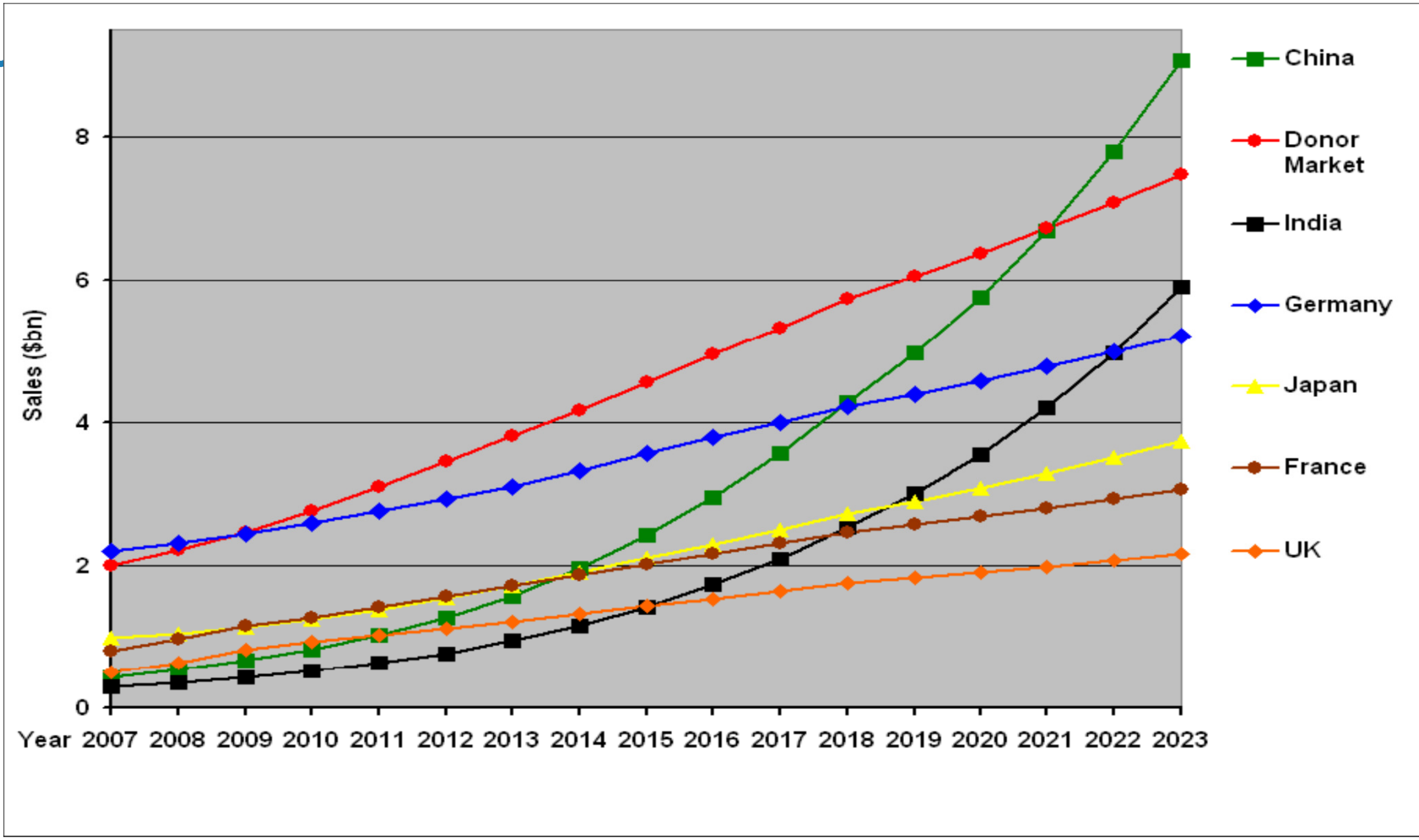
Spectacular growth rate : 10 - 15% per year versus 5-7 % for Pharmaceuticals



Sources: different estimates and projections (WHO, Industry, Frost and Sullivan, Biomarket group, Bionest, Kalorama,.)

2009-2012: projections

Market Growth Predictions



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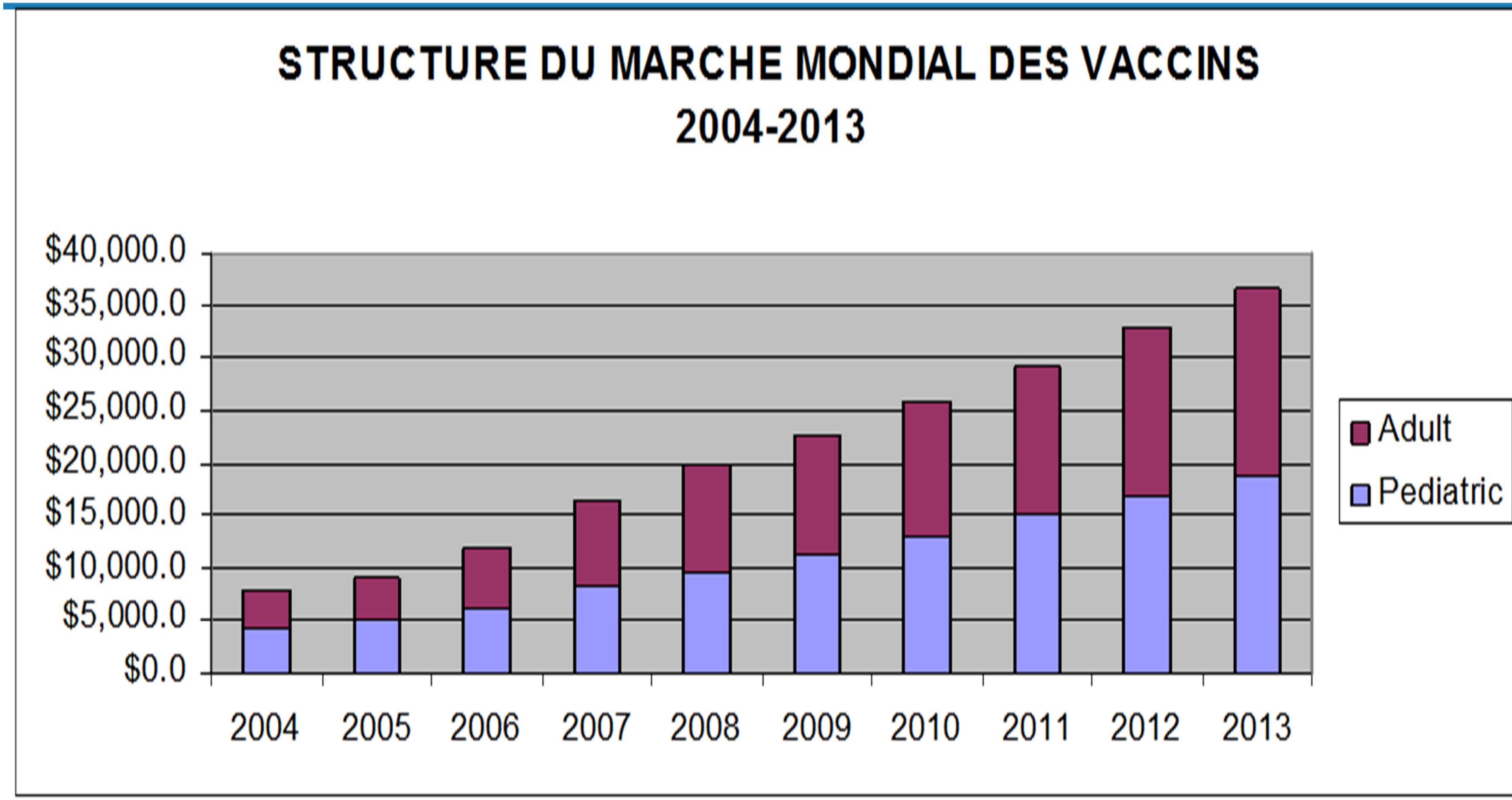
Vaccine segments

- Human vaccines
  - Pediatrics
  - Adolescents
  - Adults
  - Elderly

Value of Adult and Pediatric Vaccines



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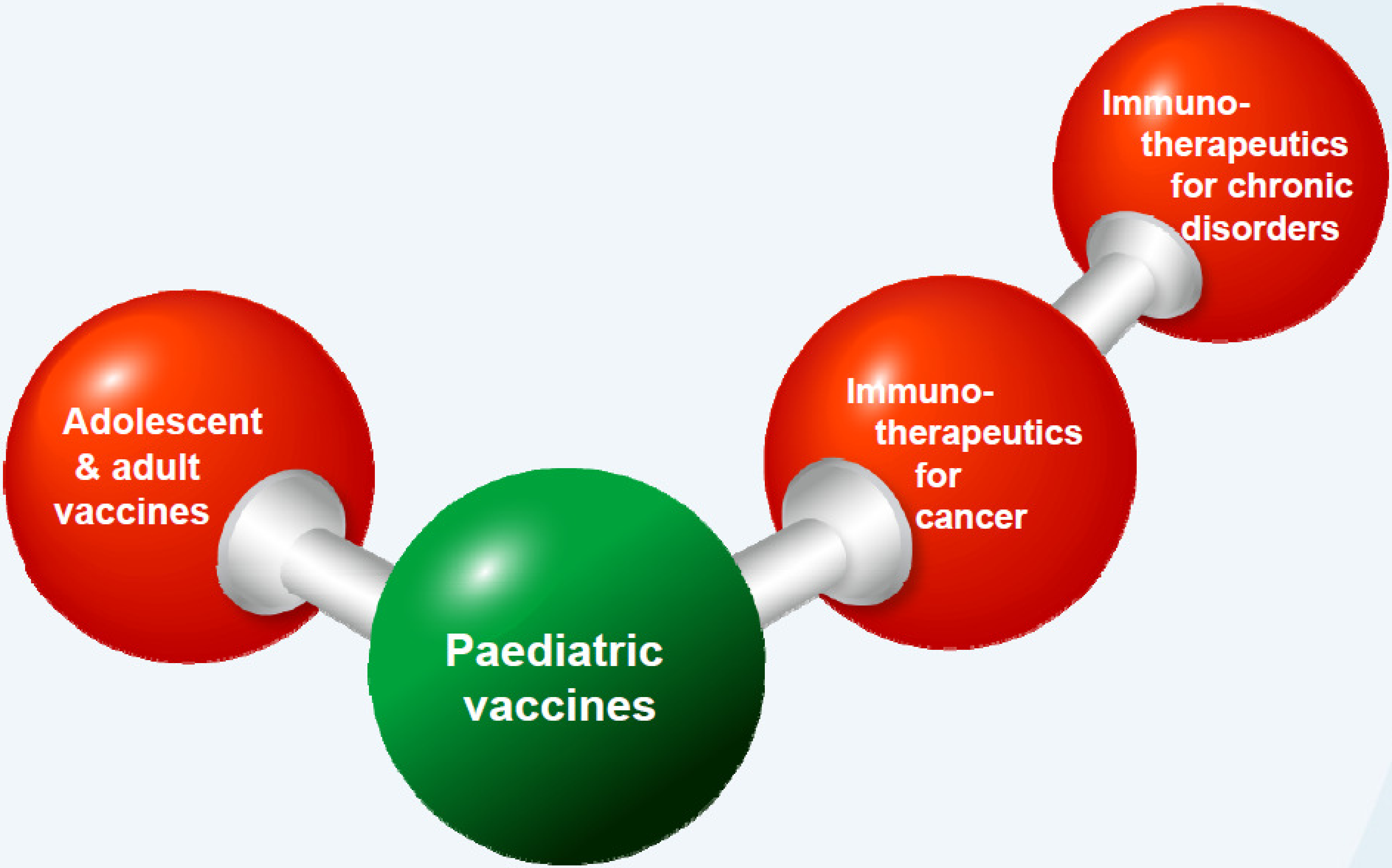
Vaccines For Humans Have Been Developed against ~25 infectious diseases

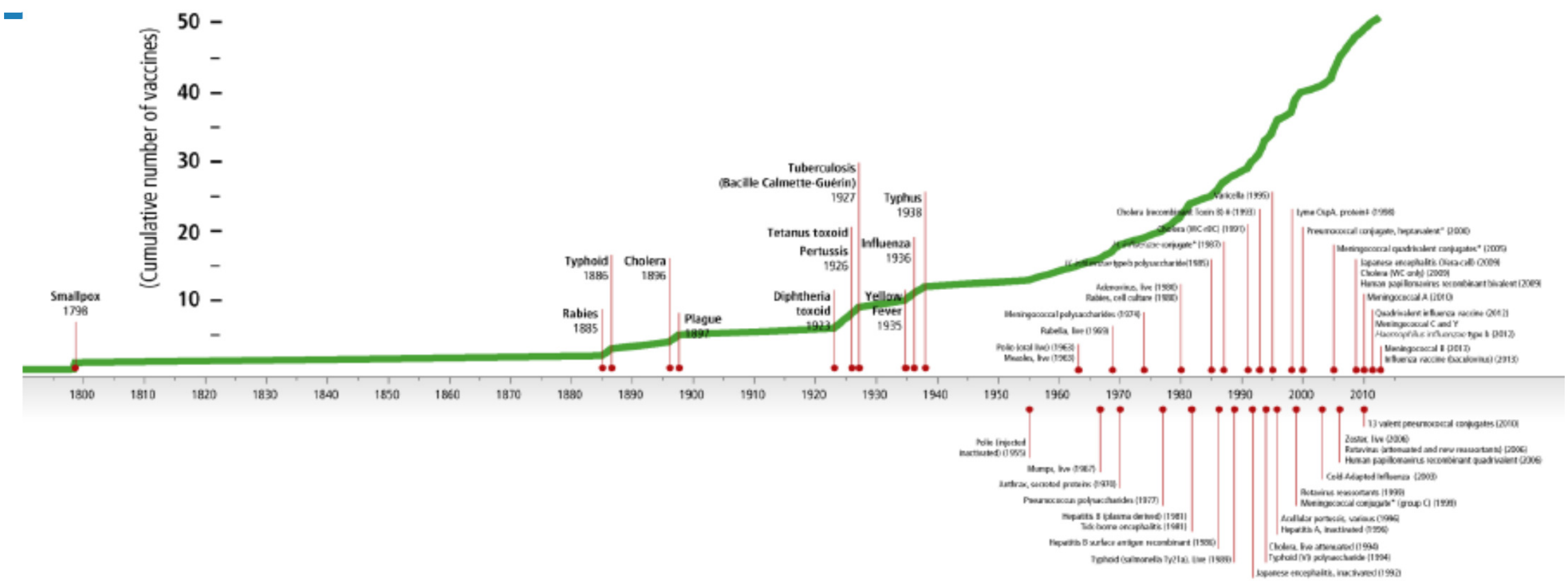
- ***Bacterial diseases:***
  - Whooping cough
  - Diphtheria
  - *Haemophilus influenzae b* infections
  - Meningococcus meningitis
  - Pneumococcal infections
  - Tetanus
  - Tuberculosis
  - Typhoid fever
  - Cholera
  - Anthrax

- ***Virus diseases***
  - Yellow fever
  - Mumps
  - Poliomyelitis
  - Measles
  - Rubella
  - Influenza
  - Hepatitis A
  - Hepatitis B
  - Adenovirus
  - Rabies
  - Japanese encephalitis
  - Chickenpox
  - Papilloma viruses
  - Tick-Borne Encephalitis
  - Smallpox
  - Rotavirus

Evolution of a diversified business



Cumulative number of vaccines developed



With Thanks to Stan Plotkin

Seth Berkley

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Vaccine Market: Growth Factors?

Combination of :

- Importance of communicable diseases and new threats
- New vaccines, new presentations and indications
- Cost effectiveness of immunizations
- New funding opportunities (Gov, PPP, donors, Foundations,...)
- New research techniques and manufacturing technologies
- Increasing demand, new target population, larger emerging markets
- Higher prices, improved profitability for the industry
- "Blockbuster" sales for some innovative vaccines

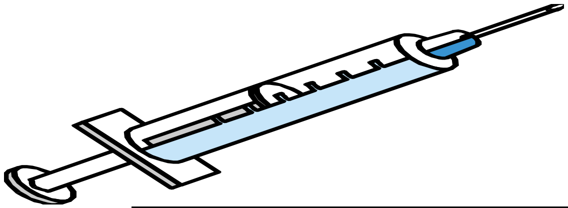
Global Vaccine Market:
Rapid Growth and Changing Status

- Value from USD 5 bn in 2000 to almost USD 24 bn in 2013
- Global market projected to rise to USD 100 bn by 2025
- More than 120 new products in the development pipeline
- 60 are of importance for developing countries

➢ Vaccines: becoming an engine for the pharmaceutical industry

➢ Changing status of the vaccines within the pharmaceutical industry

➢ New business model for vaccines is emerging?



Top product sales in 2010

Brand name (producer)	Type/composition	2010 sales (US$)
Prevnar-13 (Pfizer)	13-valent pnenumococcal conjugate vaccine	$2.4 billion
Proquad (Merck/Sanofi-Aventis)	Measles-mumps-rubella and varicella combination vaccine (MMR-V)	$1.4 billion
Gardasil (Merck)	HPV	$1.35 billion
Prevnar (Pfizer)	7-valent pnenumococcal conjugate vaccine	$1.2 billion
Fluzone (Sanofi Pasteur)	Influenza (seasonal and H1N1 strains)	$1.2 billion
Infanrix and Pediarix) (GSK)	Infanrix = DTaP Pediarix = DTap-HepB-IPV (combination DPT-based vaccines with acellular pertussis)	$1.2 billion

Source: Krishan Maggon knoll (http://knol.google.com/k/krishan-maggon/global-vaccine-market-2010/3fy5eowy8suq3/152….)

World Health Organization

Total sales 2012 (1)

	Vaccine	Company	H1 Sales	Use
1	Prevnar 13	Pfizer	$3.718 billion	Pneumonia, otitis
2	Gardasil	Merck & Co. and Sanofi Pasteur MSD	$1.900 billion	Vulvar, vaginal, cervical cancer
3	PENTAct-HIB	Sanofi and Sanofi Pasteur MSD	$1.522 billion	Diphtheria, Pertussis/whooping cough; Tetanus; Polio; Haemophilus influenza type b
4	Infanrix/Pediarix	GlaxoSmithKline	$1.183 billion	Diphtheria; Tetanus; Pertussis; Hepatitis B; Poliomyelitis
5	Fluzone	Sanofi and Sanofi Pasteur MSD	$1.152 billion	Influenza
6	Hepatitis franchise	GlaxoSmithKline	$986 million	Hepatitis A, B
7	Varivax	Merck & Co. and Sanofi Pasteur MSD	$846 million	Varicella

Sources: Genetic Engineering and Biotechnology News; 8 July 2013

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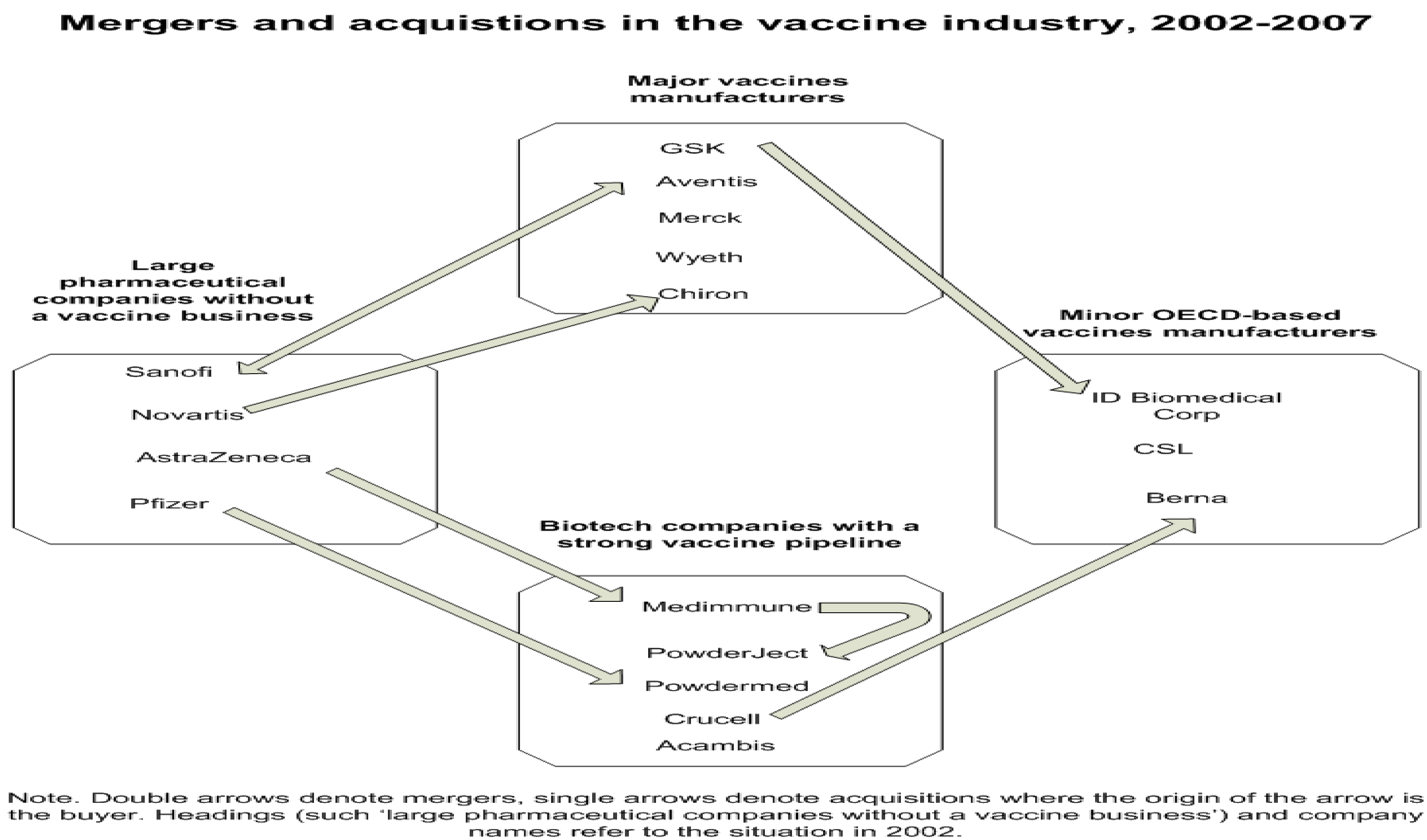
Total sales 2012 (2)

	Vaccine	Company	H1 Sales	Use
8	Menactra	Sanofi and Sanofi Pasteur MSD	$735 million	Meningococcal
9	Zostavax	Merck & Co. and Sanofi Pasteur MSD	$651 million	Shingles
10	RotaTeq	Merck & Co. and Sanofi Pasteur MSD	$648 million	Rotavirus gastroenteritis
11	Synflorix	GlaxoSmithKline	$587 million	Pneumococcal disease; Otitis
12	Pneumovax 23	Merck & Co. and Sanofi Pasteur MSD	$580 million	Pneumococcal disease
13	Rotarix	GlaxoSmithKline	$549 million	Rotavirus gastroenteritis
14	Adacel	Sanofi and Sanofi Pasteur MSD	$469 million	Diphtheria; Pertussis/Whooping Cough; Tetanus
15	Prevnar/Prevenar (7-valent)	Pfizer	$399 million	Pneumococcal disease

Sources: Genetic Engineering and Biotechnology News; 8 July 2013

New trends and features?

MERGERS AND ACQUISITIONS 2002-2007: Illustration



Overview of major vaccine related acquisitions (2005-2012)

Target Company	Acquiring Company	Investment Made	Date Announced
1. Bilthoven Bio of Netherlands	Serum Institute of India	Euros 80 mn	July 2012
2. Zhejiang Tianyuan Bio	Novartis	$125 mn?	March 2011
3. Wyeth	Pfizer	$68 bn	Jan 2009
4. MedImmune	AstraZenecea	$15.6 bn	April 2007
5. Chiron	Novartis	$5.1 bn	Oct 2005
6. Crucell	Johnson & Johnson	$2.6 bn	Sep 2009
7. ID Biomedical	GSK	$1.4 bn	Sep 2005
8. Shantha Bio	Sanofi Aventis	$781 mn	July 2009
9. Acambis	Sanofi Aventis	$549 mn	July 2008
10. Intercell	Novartis	$363 mn	July 2007
11. Corixa	GSK	$300 mn	May 2005
12. PowderMed	Pfizer	$230 mn	Oct 2006
13. Coley	Pfizer	$214 mn	Nov 2007

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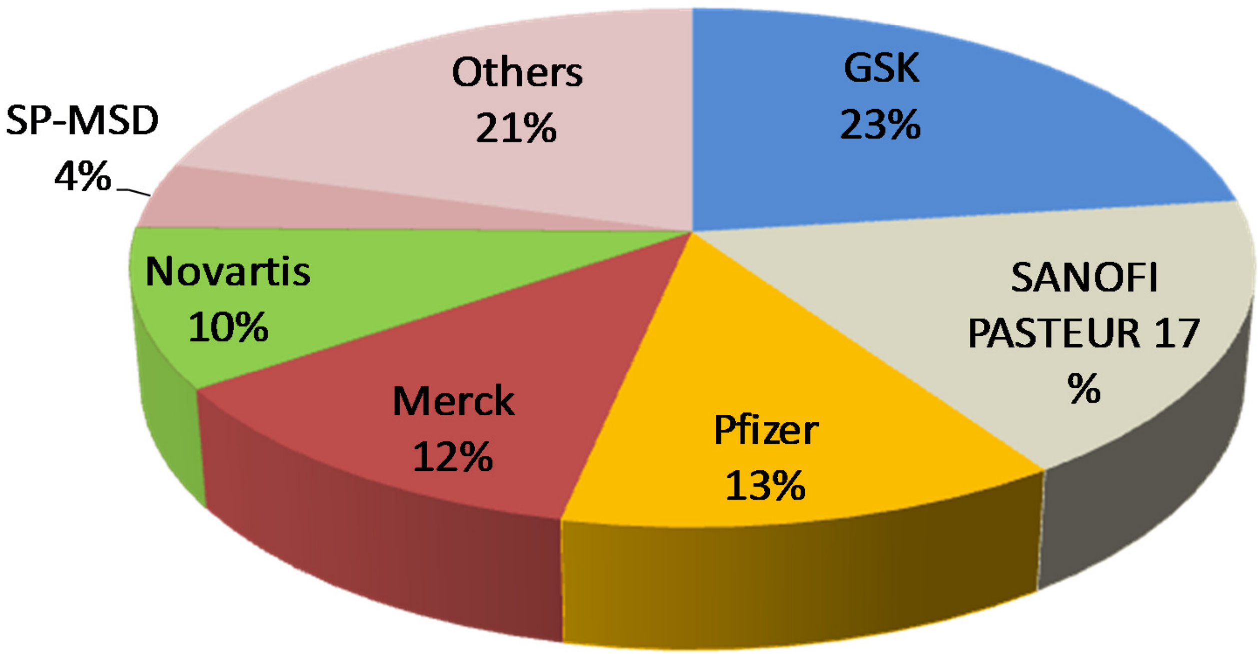
Source:VacZine Analytics + Fierce vaccine

Global vaccine leaders



- 5 large multi-national corporations make up 80% of the global market
- Major focus on new vaccine development for industrialised country markets

Newer and more expensive vaccines are coming into the market faster than ever before

- Hib containing vaccines: mono, tetra, pentavalent, hexavalent,…
- New products: PCV, RV, HPV
- New presentations and formulations: liquid/lyophilized, number of doses,…
- Vaccine pipeline: HPV *9-valent* (“nonavalent”), Malaria, TB, .. Hundreds of vaccines under development..
- Higher cost and prices

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New business MNC model is emerging?

- More mapping, market segmentation and price differentiation
- Outsourcing selected part of R&D, production and commercialization to access promising markets and local capacities, lower production costs
- Aggressive marketing, “Pharma like" model
- Risk sharing with countries and donors

UN Market: UNICEF SD and PAHO RF

Spectacular increase in the last 10 years

Both UNICEF SD and PAHO

Polio, measles, new vaccines,..

National, regional and global priority

MDGs, GIVS, GAVI, AMC, IFFim, GPEI, Measles partnership, BMGF, DOV/GVAP

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EMERGING MANUFACTURERS ARE PLAYING AN ACTIVE ROLE

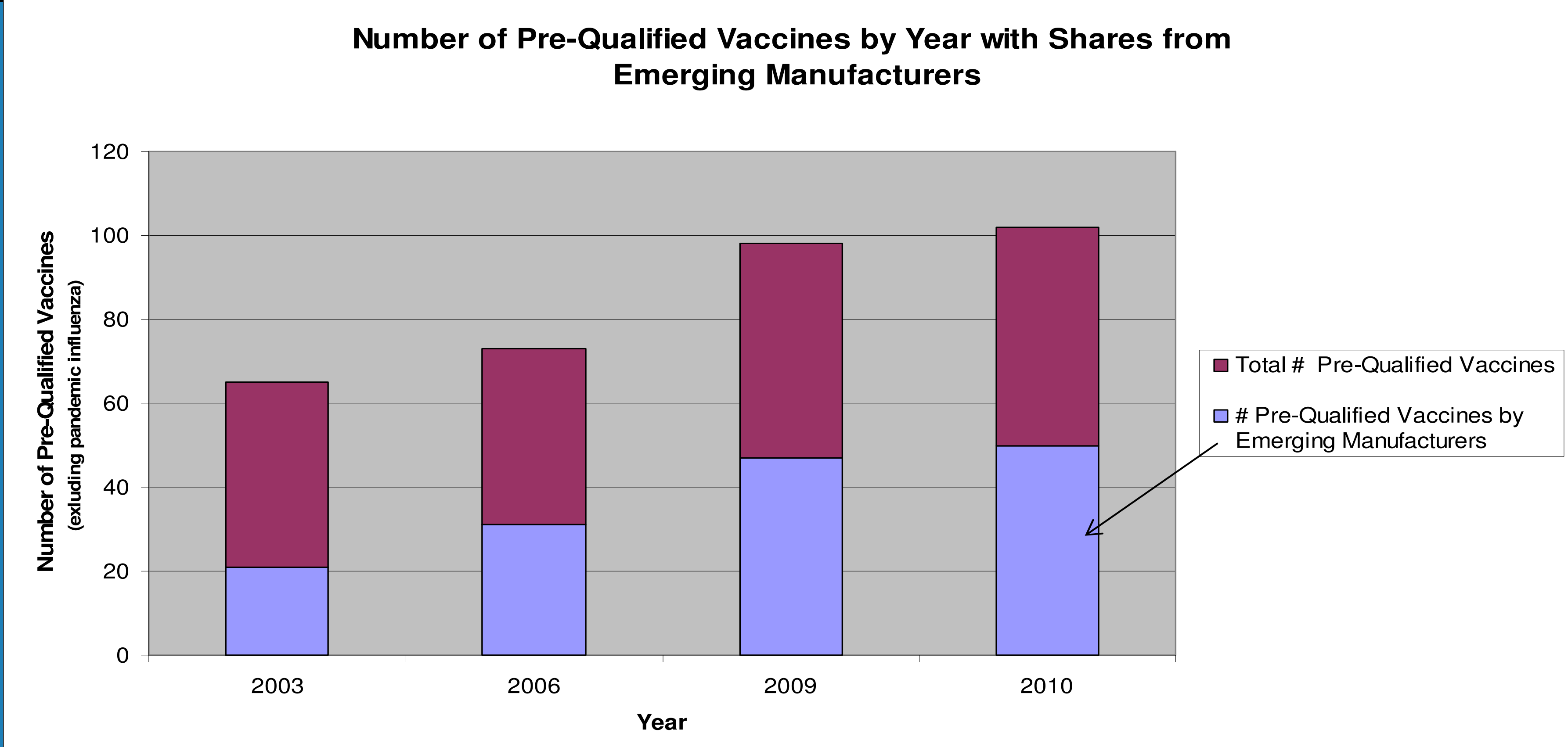
- Brazil: Bio-Manguinhos, Butantan Institute
- China: Chengdu, Shanghai (SIBP), Sinovac, Shenzhen AVP, Shenzhen Kangtai
- Cuba: CIGB, Instituto Finlay
- India: Panacea Biotec, Shantha Biotechnics, Bharat Biotech, Biological E (BE), Serum Institute of India
- Indonesia: Biofarma
- Mexico: Birmex
- Republic of Korea: Berna Green Cross (Berna), LG Life Sciences (LG)

→ **Volume, EPI vaccines, prices,...**

Emerging Market Suppliers

- Critical to competition and increased supply capacity and lowering prices
- Quality standards and requirements exactly the same as for MNC
- Emerging producers are playing a critical role in developing countries: EPI and combo vaccines
- Now supplying about 50% procurement through UNICEF by volume (less than 30% by value)
- Top country by value for UNICEF vaccine procurement 2012 - India

Year	Total # Pre-Qualified Vaccines (excluding pandemic influenza)	# Pre-Qualified Vaccines by Emerging Manufacturers (excluding pandemic influenza)	% of Pre-Qualified Vaccines by Emerging Manufacturers	# Emerging Manufacturer Countries with Functional NRA's
2003	66	21	32.3%	6
2006	73	31	42.5%	6
2009	98	47	48.0%	6
2010	102	50	49.0%	7



Source: WHO-IVB-QSS. As of September 6, 2010

GAVI's vaccine portfolio

Manufacturers with pre-qualified vaccines in 2013		Total
Pentavalent (DTP-HepB-Hib)	gsk, Crucell, Poonawalla Group, BE, LG Life Sciences	5
Rotavirus	gsk, MERCK	2
Pneumococcal conjugate	gsk, Pfizer	2
Yellow fever	Bio-Manguinhos, sanofi pasteur, Institut Pasteur	4
Meningococcal A	Poonawalla Group	1
Measles-Rubella	Poonawalla Group	1
HPV	gsk, MERCK	2

35

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New global trends?

Demand side	• Vaccines and vaccinations: on the top of Govt. and UN agenda, unmet needs • Accelerate uptake and increasing demand in Low income countries • Middle Income countries promising but challenging
Supply	• Increasing capacity • New products, presentations, indications, requirements,.. • New supply strategies • Remaining supply tensions on almost all the products
Funding	• Government resources • Donors • Private foundations • Increasing Co-financing • Others..

More players on demand, supply and financing

Potential implications for countries

1. Increased vaccine market knowledge (reducing knowledge asymmetry).
2. Information sharing on vaccine pipeline, supplier performance, quality, prices,…
3. Solid forecasting of demand.
4. Improved tendering and contracting approaches.
5. Strong quality control performing all necessary functions.
6. Flexible legislative environment.
7. Removing barriers to competition and market entry.
8. Optimised financing, payment and procurement terms to meet vaccine market dynamics.
9. Good coordination, communication and allocation of roles and responsibilities between stakeholders.